

Remarks

Claims 13-23 and 58-63 have been cancelled. New claims 66-79 have been added. Claims 1-12, 24-57, 64, and 65 have been withdrawn from consideration. Claims 66-79 are presented for the Examiner's review and consideration. Applicant believes the amendments and accompanying remarks herein serve to clarify the present invention and are independent of patentability. No new matter has been added.

Priority

Applicant has requested a certified copy of the German priority application 10139492.6 (filed on August 13, 2001) and will submit this copy to the Office when it is received.

Applicant notes that the priority claimed to international application, PCT/EP02/09082 (filed on August 13, 2002) is domestic priority and thus, submission of a certified copy of this PCT application is not required.

Amendments to the Specification

No new matter has been added by the amendments to the specification made herein. Paragraphs [0164], [0166], [0168], [0172], and [0173] have been amended only to identify the nucleotide sequences disclosed therein with the proper sequence identification numbers. These sequences were listed and assigned sequence identification numbers in the substitute Sequence listing filed on January 9, 2006. Accordingly, Applicant respectfully submits that the application satisfies Sequence Rule Compliance. Applicant further submits that the requirements for a Substitute Sequence Listing set forth in the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence are in error.

Amendments to the Claims

No new matter has been added by the addition of new claims 66-79. The subject matter of these new claims is supported by claims 13-23 and 58-63 as originally filed. Claim 66 incorporates the subject matter of cancelled claims 13, 14, and 18. New claim 67 incorporates the subject matter of cancelled claim 14 as claim 14 disclosed that the RNA encoded is for repair of mutated sequences. This new claim is also supported by the specification as originally filed at paragraph [0003]. New claim 68 incorporates the subject matter of cancelled claim 15; new claim 69 cancelled claim 16; new claim 70 cancelled claim 19; new claim 71 cancelled claim 20; new claim 72 cancelled claim 21; new claim 73 cancelled claim 23; new claim 74 cancelled claim 58; new claim 75 cancelled claim 59; new claim 76 cancelled claim 60; new claim 77 cancelled claim 61; new claim 78 cancelled claim 62; and new claim 79 cancelled claim 63.

Objection to the Specification

The specification was objected to for allegedly disclosing matter that is not in compliance with the sequence rules. Specifically, the Examiner states that Figures 1A, 9A-C, 10A-C, 12B, 13A-B, 16A-B, 17A-K, 18A-M, and 19A-E contain nucleic acid sequence which are not preceded by “SEQ ID NOs.” Additionally, the Examiner notes sequences disclosed at pages 52-56 of the specification as originally filed that are not identified by sequence identification numbers.

In response, Applicant has carefully reviewed the entire specification, figures, and previously filed Sequence Listings. The sequence rules embrace all unbranched nucleotide sequences. *See* MPEP 2421.02. The nucleotide sequences shown in the figures either contain a branched sequence or are derived from sequences containing a branched sequence. This is the “branch A” sequence which enables the formation of the lariat during RNA splicing. *See* paragraph [0049] of the published application. The “branch A” sequence is identified by an “A” in superscript or by underlining. Furthermore, the sequence rules indicate that at least 4 nucleotides be specifically defined. The sequences disclosed in the figures are shown as partial sequences or interrupted by stretches of unknown bases. Thus, Applicant respectfully submits that these sequences do not require sequence identification numbers.

However, Applicant noted that the sequences disclosed at paragraphs [0164], [0166], [0168], [0172], and [0173] were previously assigned sequence identification numbers that were not disclosed in the text of the specification. Thus, paragraphs [0164], [0166], [0168], [0172], and [0173] have been amended to identify the nucleotide sequences disclosed therein with the proper sequence identification numbers in accordance with 37 CFR 1.821(d).

In light of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the objection to the specification with regard to compliance with the sequence rules.

Objection to the Claims

Claim 58 was objected to as allegedly containing informalities. Specifically, claim 58 recites “A probe RNA-encoding DNA for t~~he~~ RNA-encoding DNA.” The Examiner requires correction.

Claim 58 has been cancelled. New claim 74 corresponds to cancelled claim 58 and does not recite the above typographical error.

In light of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the objection to the claim 58.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 14-23 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter Applicant regards as the invention. Specifically, the Examiner asserts that claims 14-23 recite the limitation “The repair RNA-encoding DNA according to claim 13” which lacks antecedent basis because claim 13 recites a “trans-splicing RNA-encoding DNA”, not the “repair RNA-encoding DNA.” Further, claim 13 does not contain any claim language pertinent to the meaning of repair.

Claims 14-23 have been cancelled. New claims 66-73 correspond to the cancelled claims and recite “A DNA encoding a trans-splicing RNA.” Further, new claim 67 clarifies that the

trans-splicing RNA encoded can be used for cellular repair of mutated exons of RNA. *See* paragraph [0003] of the published application.

Thus, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 102 (a), (b), and (e)

Claims 13-17, 19, 21, 22, 58-60, 62, and 63 were rejected under 35 U.S.C. § 102 (a) and (b) as allegedly being anticipated by Mitchell (U.S. Patent 6,013,487; hereinafter “Mitchell”).

Claims 13-15 and 58 were rejected under 35 U.S.C. § 102 (e) and as allegedly being anticipated by Sullenger et al. (U.S. Patent 6,897,016 B1; hereinafter “Sullenger”).

Claims 13-15, 21, 22, 58-60, and 62 were rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by Puttaraju et al. (Nature Biotechnology 17:246-252 1999; hereinafter “Puttaraju”).

For reasons set forth below, Applicant respectfully submits that these rejections should be withdrawn.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). *See* MPEP 2131.

Independent claims 66 and 77 recite, *inter alia*, a DNA encoding an RNA with splice sites having a branch A site including an 8-mer sequence U-A/G-C/U-U-A/G-A-C/U-A/G and a polypyrimidine base stretch having a sequence of 15 to 18-mer (U/C). None of the cited references (Mitchell, Sullenger, and Puttaraju) teach an RNA including these characteristic sequences. Therefore, the cited references do not teach each and every element of the invention as currently claimed in independent claims 66 and 77.

Accordingly, independent claims 66 and 77 are not anticipated by Mitchell, Sullenger, or Puttaraju. As claims 67-76, 78, and 79 depend from claim 66, these dependent claims

necessarily include all the elements of their base claim. Thus, Applicant respectfully submits that the dependent claims are allowable over Mitchell, Sullenger, or Puttaraju for at least the same reasons.

In light of the foregoing, Applicant respectfully requests reconsideration and withdrawal of these rejections of the claims under 35 U.S.C. § 102 (a), (b), and (e).

Rejection under 35 U.S.C. § 103(a)

Claims 13-23 and 58-63 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Puttaraju et al. (Nature Biotechnology 17:246-252 1999; hereinafter “Puttaraju”) in view of Reyes et al. (RNA 2:213-225 1996; hereinafter “Reyes”); Caudevilla et al. (Nucleic Acids Research 29(14):3108-3115 2001; hereinafter “Caudevilla”); and Bruzik et al. (PNAS USA 92:7056-7059 1995; hereinafter “Bruzik”). Claims 13-23 and 58-63 have been cancelled. New claims 66-79 correspond to the cancelled claims. For reasons set forth below, Applicant respectfully submits that this rejection should be withdrawn.

The Examiner asserts that Puttaraju do not teach a trans-splicing DNA construct comprising a GU dinucleotide at the 5' splice site, or that the 5' has the 6-mer sequence of “GUAAGU”, or at least one ESE sequence. However, Reyes, Caudevilla, and Bruzik teach these missing elements. The Examiner concludes that it would have been obvious to one of ordinary skill at the time of the invention to add the missing elements as taught by Reyes, Caudevilla, and Bruzik to the constructs of Puttaraju to arrive at the instant invention.

Applicant respectfully disagrees. Reyes, Caudevilla, and Bruzik do not remedy the deficiencies of Puttaraju noted above in the response to the rejections under 35 U.S.C. 102. While adding such elements may increase the efficiency of the trans-splicing reactions capable of gene repair, the rate of cis-splicing and/or trans-splicing with sequences not targeted for repair may not be concurrently reduced as is with the construct of the instant invention. Thus, one of skill in the art would have no reason to attempt to improve the construct as taught by Puttaraju.

Accordingly, Applicant respectfully submits that independent claims 66 and 77 are patentable over Puttaraju, Reyes, Caudevilla, and Bruzik. As claims 67-76, 78, and 79 depend from claim 66, these dependent claims necessarily include all the elements of their base claim.

Thus, Applicant respectfully submits that the dependent claims are allowable over Puttaraju, Reyes, Caudevilla, and Bruzik for at least the same reasons.

In light of the foregoing, Applicant respectfully requests reconsideration and withdrawal of these rejections of the claims under 35 U.S.C. § 103 (a).

Conclusion

In light of the foregoing amendments and remarks, this application is now in condition for allowance and early passage of this case to issue is respectfully requested. If any questions remain regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned. A fee for a three month extension of time pursuant to Section 1.17(a)(3) in the amount of \$555 is believed to be due and is being paid via credit card. No other fees are believed to be due at this time. However, please charge any other required fee (or credit overpayments) to the Deposit Account of the undersigned, Account No. 500601 (Docket No. 7700-X04-013).

Respectfully submitted,

/Paul D. Bianco/

Paul D. Bianco, Reg. # 43,500

Customer Number: 27317
FLEIT GIBBONS GUTMAN BONGINI & BIANCO P.L.
21355 East Dixie Highway, Suite 115
Miami, Florida 33180
Tel: 305-830-2600; Fax: 305-830-2605
e-mail: pbianco@fggbb.com